CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76268

ADMINISTRATIVE DOCUMENTS

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: **76-268** Date of Submission: **October 29, 2001**

Applicant's Name: **Jerome Stevens Pharmaceuticals**

Established Name: **Digoxin Tablets USP, 0.125 mg and 0.25 mg**

Labeling Deficiencies:

1. CONTAINER 100s and 1000s

   a. "mcg" rather than

   b. Add "(see USP)" to the storage temperature recommendations.

   c. The Poison Prevention Packaging Act states that special packaging (child-resistant closures) should be the responsibility of the manufacturer when the container is clearly intended to be utilized in dispensing (unit-of-use packaging). Your proposed containers of 100 appear to be in this category. Therefore, we believe that this package must comply with the Act. We further note that the 100s container size for the reference listed drug is marketed with a child-resistant closure. Please comment.

   d. 21 CFR 201.1 (h) (2) states that if a name appears on a labeling piece without qualification that it implies that they are the sole manufacturer. We note that "USP, Inc." appears on your container labels without qualification. Please comment and/or qualify/delete "USP, Inc.".

2. INSERT

   a. GENERAL COMMENT

      There is no need to capitalize "Digoxin" throughout the package insert unless required by sentence structure.

   b. DESCRIPTION

      i. Second paragraph, chemical name - The "O's" should be in *italics*.

      ii. Last paragraph - You may delete the after each inactive ingredient.

      iii. We encourage you to list the inactive ingredients in alphabetical order.

   c. CLINICAL PHARMACOLOGY

      i. Mechanism of Action, number (2) - "renin-angiotensin" (add hyphen)

      ii. Table 1, footnote - "100 mcg" and "125 mcg" (delete the hyphens)

      iii. Table 2, last column heading - Replace the "+" with a " * ".

iv. Chronic Heart Failure, second paragraph, third line - Replace the "=" with a "≤".

v. Table 3, first column - Replace the "='s" with "≤'s".

d. OVERDOSAGE

Massive Digitalis Overdosage

i. First paragraph, first sentence - "bradyarrhythmias" (delete hyphen)

ii. Third paragraph, third sentence - "patients" rather than "patient's"

e. DOSAGE AND ADMINISTRATION

i. Serum Digoxin Concentrations, number "5" - Decrease the space between "acutely" and "during"

ii. Heart Failure

A). Number "2" - Decrease the space between "will" and "take".

B). Rapid Digitalization with a Loading Dose, fourth paragraph, last sentence - "70 kg" (delete hyphen)

C). Maintenance Dose, third paragraph, last line - "m^2" rather than "m2"

D). Table 5, footnote, first line - "*For adults*" (*italics*)

iii. Dosage Adjustment When Changing Preparations, last paragraph - Delete the hyphens before "mcg" and "mg"

f. HOW SUPPLIED

i. We note that you have described your tablets as having the imprints "JSP-544" (0.125 mg) and "JSP-545" yet on pages 4629 and 4630 you have them described as having the imprints "DP 914" (0.125 mg) and "DP 915" (0.25 mg). Please comment and revise if necessary.

ii. Please revise your storage temperature recommendations to be consistent with those as seen on your container labels. See also comment (b) under "CONTAINER".

iii. Add the "Dispense in ..." statement as seen on your container labels.

Please revise your container labels and insert labeling, as instructed above, and submit 12 copies of each labeling piecE in final print.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes - http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

/S/

Wm. Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research